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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1639	
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12/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,892	AKOPIAN ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *10 and 13-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/26/2007;10/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Office Action Appendix*.

DETAILED ACTION

The examiner on the present case has changed. See contact information below. Responsive to communications entered 9/23/2009. Claims 1-30 are pending. Claims 10,13-30 are withdrawn. Claims 1-9,11,12 are examined herein.

Election/Restrictions

Applicant's election without traverse of invention/group I, drawn to a method of making a cDNA expression library in the reply filed on 9/23/2009 is acknowledged.

Claims 13-30 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/23/2009.

Applicant's election without traverse of trigeminal ganglion neurons for the species of neuron in the reply filed on 9/23/2009 is acknowledged.

Claims 10 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/23/2009.

Priority

The present application is a 371 of PCT/US05/08064 filed 03/09/2005 which claims benefit of 60/551,741 03/10/2004.

Information Disclosure Statement

The information disclosure statement filed 3/26/2007 fails to comply with 37 CFR 1.98(b)(5) because it does not include a the publication date, author, etc. It has been

placed in the application file, but the information referred to therein regarding citation A73 has not been considered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3,5-6,8 are rejected under 35 U.S.C. 102(a or e) as being anticipated by **Heintz et al** (WO 03/038049; IDS entry 10/14/2008).

The claimed subject matter per claim 1 is drawn to a method of making a cDNA expression library enriched for cDNAs that encode secretory or membrane-bound proteins, comprising the steps of:

a. isolating membrane bound polysomal RNA from a selected population of cells;
b. isolating polyadenylated RNA from the isolated membrane-bound polysomal RNA from step (a);
c. constructing a cDNA expression library from the isolated polyadenylated RNA from step (b),

wherein the cDNA expression library comprises more than 90% cDNAs that encode secretary and membrane-bound proteins

Claims 2-3,5-6,8 constitute variations of the above.

Heintz et al teach, throughout the document and especially the title and abstract, a method for isolating particular cell type mRNAs by isolating tagged ribosomes plus the mRNAs bound thereto.

On p 7 line 17, p 44 line 26 and the description to figure 1, Heintz teach isolating membrane bound polysomal RNA from a selected population of, for instance, rat brain cells (neurons), reading on claims 1a and 8. On p 46 lines 30-31, Heintz et al teach isolating polyadenylated mRNA by means such as oligoT cellulose, reading on claim 1b and 5. On p 116 lines 11-13, Heintz et al teach converting said mRNA into a cDNA library, reading on claim 1c. On p 3 lines 34-35, Heintz et al teach an embodiment to isolate mRNAs encoding secreted or membrane bound proteins and on p 2 lines 25-26 Heintz et al disclose the compositions which comprise as much as 99 % of the tagged ribosome and its associated mRNA (which, as mentioned above may be converted to cDNA), therein reading on “wherein the cDNA expression library comprises more than 90% cDNAs that encode secretary and membrane-bound proteins” of claim 1.

On p 44 steps (2-4), Heintz et al teach homogenization buffers using high salt concentrations lacking detergent followed by centrifugation through sucrose, reading on claims 2-3.

On p 188 line 5, Heintz et al teach employing the pCDNA3 vector, reading on claim 6.

Claims 1,5 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by **Tsuchiya et al** (US Patent 6610485 – PTO 892 7/23/2009).

Tsuchiya et al teach, throughout the document and especially the abstract and column 2 line 57 through column 3 line 5, a method of selectively isolating genes encoding membrane-bound proteins using a cDNA library fused to a secretory protein fused to an antigen. Following transfection, clones encoding membrane-bound fusion proteins which bind an antibody raised against said antigen are selected and the cDNA isolated.

Tsuchiya et al teach in column 6, the use of whole mRNA/cDNA libraries from cells such as neurons, which is taken as including polysomal RNA from a selected population of cells as set forth in claim 1a. In the same passage, Tsuchiya et al teach isolation of poly A mRNA using a Pharmacia (now GE Healthcare) QuickPrep mRNA kit which includes cellulose oligo dT , as evidenced by the QuickPrep mRNA manual included as an appendix to this office action, thus reading on claims 1b and 5. As mentioned above, said cDNA is used to express membrane-bound proteins, reading on claim 1c. Absent evidence to the contrary, said clonal selection provides 100% cDNAs that encode secretary and membrane-bound proteins.

Said neurons read on claim 8.

Therefore, the claims are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3,5-6,8 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Heintz et al** (WO 03/038049; IDS entry 10/14/2008) in view of **Cardelli et al** (1977 Biochemistry 16:5127-5134 – IDS entry 3/26/2007).

Heintz et al is relied on as above.

Heintz et al do not teach inverted ultra-centrifugation, such as set forth in claim 4.

Cardelli et al teach, throughout the document and especially the title and abstract, isolation and characterization of free and membrane bound polysomal mRNAs from rat liver.

In figure 3, Cardelli et al teach sucrose gradient ultra-centrifugation at 40,000 rpm for 5 h hours using a SW41 swing out rotor, such as discussed in paragraph 0065 of the present published application and used in paragraph 0177 of the present published application. In the same passage, Cardelli et al teach ultracentrifugation both with and without sodium dodecyl sulfate (SDS; a detergent), the latter of which further reads on claim 3.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to analyze the tagged polysomal RNAs according to Heintz et al with the inverted ultra-centrifugation method described by Cardelli et al.

One of ordinary skill in the art would have been motivated to analyze the tagged polysomal RNAs according to Heintz et al with the inverted ultra-centrifugation method described by Cardelli et al because it would allow the skilled artisan to better characterize the RNAs (i.e. identify various ribosomal components) as discussed by Cardelli et al on p 5129 right column first full paragraph and the paragraph bridging pp 5132-5133.

One of ordinary skill in the art would have had a reasonable expectation of success in applying the inverted ultra-centrifugation taught by Cardelli et al toward the tagged ribosomes of Heintz et al because both references concern polysomes and centrifugation thereof. Thus the technique of Cardelli et al lies well within the scope of technology according to Heintz.

Claims 1-3,5-6,8 and 7,9,11,12 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Heintz et al** (WO 03/038049; IDS entry 10/14/2008) in view of **Presta et al** (US Patent Application 20020146416).

Heintz et al is relied on as above.

Heintz et al do not teach the expression vector pRK7 as set forth in claim 7 or neurons such as trigeminal ganglion neurons from claims 9,11,12.

Presta et al teach, throughout the document and especially the abstract and paragraphs 0003-0010 characterization of the trk family of neurotrophin receptor tyrosine kinases (membrane-bound) which play a crucial role in the development and maintenance of the nervous system.

For instance, in paragraph 0335 and figure 7A Presta el al teach trkA is expressed in trigeminal ganglion neurons, reading on claims 9,11,12. In paragraph 0352, Presta et al teach expression of various trkC truncations in human embryonic kidney cells using a pRK7 vector, reading on claims 6 and 7.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use the tagged ribosome technology developed Heintz to analyze trk expression throughout the nervous system per Presta.

One of ordinary skill in the art would have been motivated to use the tagged ribosome technology developed Heintz to analyze trk expression per Presta because it provides facile isolation of gene transcripts without the need to isolate individual cells or cell types, which is a difficult undertaking given the complexity of many tissues such as the nervous system, as mentioned by Heintz et al on p 1 lines 6-28.

One of ordinary skill in the art would have had a reasonable expectation of success in using the tagged ribosome technology of Heintz et al in evaluating trk expression per Presta et al because both references concern expression profiling in the nervous system. In other words, the technology developed by Heintz et al is well suited toward discerning trk expression.

In conclusion, the claimed invention was within the ordinary skill in the art to make and use at the time the claimed invention was made and was as a whole, *prima facie* obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571 272 0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1639